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Recurrence of non-invasive intraductal papillary municious neoplasm seven years following total pancreatectomy

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ABSTRACT

INTRODUCTION: Intraductal papillary mucinous neoplasm is an increasingly recognized disease with varying premalignant potential and unclear incidence, characterized by a mucin-producing epithelium and dilation of the pancreatic duct.
PRESENTATION OF CASE: We present the first documented case of distant intestinal intraductal papillary mucinous neoplasm recurrence following total pancreatectomy for side-branch non-invasive borderline malignant intraductal papillary mucinous neoplasm.
DISCUSSION: We review the current literature in order to try and answer important questions regarding our ability to predict intraductal papillary mucinous neoplasm recurrence, our understanding of the potential for recurrence and what follow-up should be recommended to properly monitor recurrence after a benign, albeit borderline malignant, side-branch lesion resection.
CONCLUSION: Our case report confirms that the low risk classification of an intraductal papillary mucinous neoplasm lesion even after total pancreatectomy does not always predict recurrence and that definitive prognostic factors of recurrence in the setting of non-invasive disease have yet to be identified. A vigilant long-term approach to follow-up may thus be required even in low risk cases

1. Introduction

Intraductal papillary mucinous neoplasm (IPMN) is a rare disease of increasing but unclear incidence.[1–3] It occurs more frequently in men in their sixth to seventh decade[1] and patients most commonly present with abdominal pain, acute pancreatitis, weight loss, new onset of diabetes, jaundice and exocrine insufficiency.[1] The lesion is characterized by mucin-producing epithelium displaying a papillary architecture and is associated with dilation of the pancreatic ducts. It can be classified anatomically as main-branch, side-branch or mixed depending on the location of the main lesion and the dilation of the pancreatic ducts on imaging. It may also histologically be invasive or non-invasive. Depending on anatomical, histopathological classification, and patient factors, an IPMN can be managed with observation or surgical resection.[1] The 5-year survival rate of cases selected for operation ranges from 36 to 77% depending on the original presence of a primary or metastatic malignancy.[4] Recurrence is seen in 7–43% of cases depending on the histopathological characteristics of the lesion.[1]

When the anatomical classification of a lesion points toward a low malignant potential, for example with an asymptomatic side-branch cystic lesion without mural nodule or main branch dilation, it is possible to manage IPMN conservatively, with yearly imaging.[5] However, the potential for malignancy associated with main duct IPMN usually warrants its removal.

2. Case report

We present the case of a 76-year-old man diagnosed with IPMN in May 2004. A CT scan at the time showed a 10 cm multicystic mass extending to the pancreas head and body with duct dilatation up to the tail. The presence of a mucinous tumor of the pancreas, possibly a side-branch IPMN, was subsequently confirmed by a magnetic resonance cholangiopancreatography (MRCP) and endoscopic ultrasound (EUS). The patient's CA19-9 level was not available at the time. Pre-operative biopsies were unsuccessful, but malignancy was suspected. In July 2004, at laparotomy, most of the pancreas and the posterior wall of the stomach formed a large mass and so the patient underwent a total pancreatectomy, cholecystectomy, gastric antrectomy and splenectomy with a hepaticojejunostomy and gastrojejunostomy. Intra-operative frozen sections showed dysplastic mucosa of the main cyst wall, and could not rule out cancer. The final pathology showed a non-invasive, well-differentiated IPMN with clear margins and ten resected lymph nodes free of tumor. The specimen was described as "borderline malignant" due to its size (10.5 cm at its largest diameter)

Abbreviations: IPMN, intraductal papillary mucinous neoplasm; MRCP, magnetic resonance cholangiopancreatography; EUS, endoscopic ultrasound.

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and exhibited pancreatic intraepithelial neoplasia (PanIN) grades I to III.

The patient was then followed with yearly serum CA19-9 levels, as well as yearly thoracoabdominal imaging. He remained asymptomatic. On CT imaging in 2010, suspicious tissue nodularities were noted in the hilum of liver. A PET-CT revealed a hypermetabolic focus (SUV of 8.6) at the site of the surgical clips in the region of the choledochojejunostomy. The patient then underwent balloon enteroscopy of the afferent hepaticojejunal limb that revealed a large small bowel polypoid mass near the hepaticojejunostomy with no signs of common bile duct obstruction. Biopsies were found to be consistent with recurrent IPMN. An abdominal MRI confirmed the presence of a 12 mm × 16 mm intra-luminal lesion at the suspected location with no extension beyond the bowel wall. No other changes or suspicious lesions were found. Over the next months the original and the newer pathological slides were extensively reviewed, as the patient was reticent to undergo operation. In January 2011 a whole body PET scan demonstrated a decrease in the metabolic activity of the mass (SUV of 5.7 from 8.6) and no new lesions. An MRCP showed interval enlargement of the lesion (23 mm × 16 mm) with no evidence of biliary obstruction. Given the interval enlargement of the lesion, the patient agreed to operation and underwent a small bowel resection with revision of the hepaticojejunostomy to the level of the hepatic duct bifurcation. Pathology revealed a recurrence of non-invasive IPMN and the margins of resection were once again negative. Following an uneventful operation, the patient remains symptom-free.

3. Discussion

This is the first description of an extra-pancreatic recurrence of a side-branch non-invasive IPMN following total pancreatectomy. Masaya et al. previously reported in a 74 years old man a recurrence of a non-invasive IPMN in the stomach after partial pancreatectomy.[6] The pattern of spread of IPMN was attributed to the presence of a fistula from the remnant pancreas. However in the present case, there was no pancreaticoenteric anastomosis, and no pancreas gland remained, making the source of recurrence a mystery. Enteric spread at the time of the original surgery and slow subsequent growth remains a hypothetical possibility.

Our case report raises an important question regarding our ability to predict IPMN recurrence based on histopathologic and anatomical classification. It also raises questions regarding our understanding of the potential for recurrence of IMPN and what follow-up should be recommended to properly monitor recurrence after a benign, albeit borderline malignant, side-branch lesion resection.

IPMN lesions are classified based on their morphological and histologic features. MRCP or EUS are initially used in order to demonstrate the side branch communication needed to make the diagnosis. CT can be used thereafter as a primary modality for preoperative characterization.[4,7,8] The prediction of the IPMN variant can be limited when using a CT scan[8] and the use of adjunct imaging modalities such as MRI, MRCP and ERCP can help better characterize the lesion.[4,8] A dilated main pancreatic duct with a diameter of 10 mm points toward a main duct IPMN.[5,7–9] On the other hand when the main duct is of normal size and a side-branch communication is visualized, a branch duct IPMN variant is suspected.[4,7,9] It is however possible for a branch-duct lesion to be multifocal and involve the entire pancreas,[5,10] as in the current case. This type of lesion needs to be carefully differentiated from the mixed IPMN variant in which there is a combination of imaging features from both main and branch duct IPMN.[7] The latter is considered to be a variant of main duct IPMN and thus known to have a greater potential for malignancy associated with the main duct lesion. Histologically, lesions are graded as low/benign, intermediate/borderline, or high-grade dysplasia/carcinoma with or without presence of invasiveness. Once invasiveness is confirmed, the histological IPMN subtype identifies a distinct probability of progression to pancreatic cancer with the pancreatobiliary, intestinal, gastric foveolar and oncocytic subtypes having the highest malignant potential and the tubular subtype the least.

The main duct IPMN variant is three times more likely to be invasive than the branch type[8] and is associated with cancer in 60–83%.[11] Current recommendation is therefore to resect all main duct and mixed IPMN variants.[5] The guidelines for branch duct IPMN allow for a more conservative approach since this lesion seems to be associated with a malignancy rate of 6–46%.[5] Therefore observation is possible in many cases, typically for lesions measuring less than 30 mm with no mural nodules, and asymptomatic elderly patients with multiple comorbidities.[5,8] Such patients can be followed with regular imaging, including ultrasound[5,8,12–14] and appearance of symptoms or signs of malignant changes mandate a surgical intervention.[5] In the case of our patient, the presenting symptoms as well as the size and intraoperative appearance of the lesion were suggestive of malignancy and prompted a surgical resection upon diagnosis.

Depending on the segment of the pancreas involved, a partial or total pancreatectomy should be performed. Total pancreatectomy is reserved for healthy patients with diffuse multi-centric disease,[15,16] as in our patient. Current treatment recommendations suggest assessment of resection margins with intra-operative frozen section in order to ensure that the totality of the dysplastic lesion has been removed.[4,5,17,18] This standard is debated as multiple studies have shown poor correlation between margin status and recurrence in the remnant pancreas in cases of non-invasive IPMN.[4,5,17–24]

Though there are no prospective comparative data, current recommendations for surveillance following resection of benign IPMN are for yearly CT or MRI, with decreased spacing over several years.[5,25] Authors suggest that the imaging strategy after resection should be based on the presence or absence of invasive disease because of implications for recurrence rate: 90% recurrence within 3 years of surgery for an invasive lesion versus 0–8% in the non-invasive setting.[7,11] Total pancreatectomy however, seems to effectively prevent recurrence of non-invasive IPMN disease.[16–24] Stauffer et al.[15] followed 47 patients after total pancreatectomy for different non-malignant pancreatic pathologies. Twenty one total pancreatectomies were performed for non-invasive IPMN: 11 simple adenomas, 1 low-moderate dysplasia, and 10 high-grade dysplasias. No recurrence was found after a mean follow-up period of 23 months. Chari et al.[18] and Passot et al.[11] confirmed the absence of recurrence after total pancreatectomy for non-invasive disease. Both authors concluded that regular surveillance imaging during follow-up was not necessary in this particular setting and should only be performed if symptoms were to appear. Such a policy in the present case would have failed to identify IPMN recurrence and growth. Given the unusual context of this case, the use of FDG-PET was aimed at ruling out the possibility of multiple sites of recurrence. This modality was more accurate than CT or MRI in distinguishing benign from malignant lesions in 64 patients with suspected IPMNs studied prospectively.[26]

4. Conclusion

This report confirms the lacks of prediction of the classification of low-risk IPMN lesion. It reminds us how little is known about the exact pattern by which extra-pancreatic spread occurs and how poorly we understand the malignant potential of IPMN. Definitive predictors of recurrence of non-invasive disease have yet to

be identified. A vigilant long-term approach to follow-up may thus be required even in low risk cases.

Conflict of interest

None.

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Ethical approval

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Author contributions

NMCD reviewed the literature, gathered the patient's information and wrote most of the article. SD and JSB were also major contributors in writing the manuscript. All authors read and approved the final manuscript.

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